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PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Arne E. Brandstrom

Serial No.: 854,739 Examiner: J. T. Fan

Filed : April 21, 1986 Group Art Unit: 121

For : NOVEL COMPOUNDS

July 30, 1986

APPLICANT'S INTERVIEW SUMMARY

Hon. Commissioner of Patents and Trademarks

Washington, D.C. 20231

Sir:

Applicant thanks Examiner Fan for granting an interview to their attorney on July 24, 1986. This paper will summarize that interview.

The captioned application is a file-wrapper continuation of U.S. Patent Application Serial No. 640,020. The parent application had been rejected over European Patents No. 5,129 and 45,200 which disclose neutral omeprazole, and U.S. Patent 4,472,409 to Senn-Bilfinger and an excerpt by Elderfield disclosing base addition salts of other compounds. Based on these references, the Examiner rejected the claimed base addition salts of omeprazole as obvious.

In response, applicant submitted two declarations which showed omeprazole salts to be surprisingly more stable than neutral omeprazole when stored as a solid, and that sodium omeprazole was some 25 times more stable in solution than a sodium trifluoromethyl derivative disclosed in Senn-Bilfinger. Based on the scope of the tests and a disagreement with the nature of the tests and the interpretation of

the data, the Examiner found that the first of these declarations was not persuasive.

At the interview, applicant's attorney presented and discussed a new declaration comparing solid state stability of neutral omeprazole and several base addition salts of omeprazole. That declaration by Ake G. Pilbrant is made formally of record herewith.

As discussed at the interview, neutral omeprazole and base addition salts were tested for stability under elevated temperature and humidity. This is a conventional methodology for determining compound shelf life, as it substantially accelerates the test procedure by shortening the testing time to a period of months from a period of perhaps years. The samples tested were evaluated by high pressure liquid chromatography (HPLC) to determine the extent of compound degradation.

The Examiner's main concern regarding the sufficiency of the data was the "equivocal" nature of the data for 1 and 3 months. These time intervals are not really significant in the present case, however, and do not accurately reflect the degradation rates of the compounds tested. As pointed out in the new Pilbrant declaration, measurements during the initial period can be inaccurate because of the presence of impurities, and because of the differing affinities of neutral omeprazole and base addition salts of omeprazole for water. The salts are hydrophilic, while neutral omeprazole is hydrophobic. For this reason, the salts will take up water faster, and degradation of the salts due to the water may start sooner than for neutral omeprazole. Over the longer time period, however, it becomes

clear that neutral omeprazole is actually degraded much faster than the basic salts.

The Examiner also objected to the scope of the declaration relative to claim 1, indicating that it only provided evidence relating to alkali metal and alkali earth salts of omeprazole, i.e., Li^+, Na^+, K^+, Mg^{++}, and Ca^{++}. Applicant does not agree with this position as there is no scientific reason why the other claimed salts would be expected to behave differently. Nevertheless, applicant's attorney agreed to limit the claims to alkali metal and alkali earth salts if this would make the pending claims allowable. Alternatively, applicant's attorney reserved the right to submit a further declaration with similar stability data relating to the other salts.

At the conclusion of the interview, Examiner Fan appeared to be convinced as to the sufficiency of the data. She indicated, however, that a further search and reconsideration of the references would be done before she would reach on opinion on the application and issue an office action.

Respectfully submitted,

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Enclosure